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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,481	01/20/2004	Nozer M. Mehta	P/546-280	2921

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
06/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,481	MEHTA ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-53,55-61 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *42,60 and 61* is/are allowed.

6)☒ Claim(s) *1-15,17-41,43-53,55-59 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The effective filing date of instant claims 1-15, 17-53, 55-61, and 63 is January 21, 2003, the filing date of provisional application 60/441,856. Instant claims 1-15, 17-53, 55-61, 61, and 63 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of the provisional application because the provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed subject matter.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-8, 12-15, 17-41, 43-47, 49-51, 55-59, and 63 are rejected under 35 U.S.C. 103(a) as being obvious over Stern et al (U.S. Patent No. 6,086,918) in view of Habener (U.S. Patent No. 5,120,712), Balschmidt et al (U.S. Patent No. 5,157,021), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742). Stern et al teach oral administration of peptides such as insulin, salmon calcitonin, parathyroid hormone, and lhrf using a carrier comprising a pH-lowering agent, an absorption enhancer, a non-physiologically active protein, a gelatin capsule, and an enteric coating. See, e.g., column 6, line 1 - column 12, line 10, and claims 1-55. Stern et al do not teach peptides which are amidated GLP-1 analogs, amidated insulin analogs, or amidated PTH analogs. Habener teaches GLP-1 analogs which are amidated. See, e.g., claims 1 and 4. Balschmidt et al teach insulin in which the carboxylic acid groups present in the sidechains at residues A4, A17, B13, and B21 are amidated in order to achieve a long-lasting protracted acting insulin analog. See, e.g., column 2, lines 5-8 and 49-53. Barbier et al teach the human parathyroid hormone derivatives hPTH(1-34)-OH and hPTH(1-31)NH_2, and teach that the derivatives can be administered orally. See, e.g., column 2, lines 26-44, and column 14, lines 59-62. The European

Patent Application '201 teaches the human parathyroid hormone derivative hPTH(1-34)NH_2. See, e.g., column 3, lines 31-36. Neiss et al teach salmon calcitonin amidated at locations which are not naturally amidated and which have extended duration of activity. See, e.g., column 1, lines 42-44, and claims 1 and 2. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al in the oral administration compositions of Stern et al because the oral administration compositions of Stern et al have general applicability to any peptide and because it would be desirable to be able to administer orally the peptides of Habener, Balschmidt et al, Barbier, the European Patent Application '201, and Neiss et al because oral administration is easier for the patient. Applicants' claims would have been prima facie obvious at the time the invention was made because applying Stern et al's known and generally applicable technique, i.e. of combining peptides with a pH-lowering agent, an absorption enhancer, a non-physiologically active protein, a gelatin capsule, and an enteric coating so that the peptides can be administered orally, to the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al, with only the expected result that the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al can be administered orally, is prima facie obvious. See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (S. Ct. 2007). With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

4. Claims 5 and 48 are rejected under 35 U.S.C. 103(a) as being obvious over Stern et al

(U.S. Patent No. 6,086,918) in view of Habener (U.S. Patent No. 5,120,712), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742) as applied against claims 1-8, 12-15, 17-41, 43-47, 49-51, 55-59, and 63 above, and further in view of Stern et al (U.S. Patent No. 5,912,014). Habener, Barbier et al, the European Patent Application '201, and Neiss et al teach known and specific peptides which are amidated at their C-termini, but do not teach synthesizing these peptides by forming glycine-extended precursors and then converting the glycine residue to a C-terminal amide group. Stern et al '014 teaches salmon calcitonin made with a C-terminal glycine extension which is enzymatically converted to an amide group. See, e.g., column 5, lines 12-23. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the known and specific peptides of Habener, Barbier et al, the European Patent Application '201, or Neiss et al for use in the oral administration compositions of Stern et al '918 by synthesizing the peptides as glycine-extended precursors and then converting the glycine residue to a C-terminal amide group, because Stern et al '014 teach that this is a known reaction technique for forming a C-terminally amidated peptide, and because the particular method of synthesizing a peptide would not have been expected to affect the in vivo activity of the peptide.

5. Claims 1-15, 17-41, 43-47, 49-53, 55-59, and 63 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 02/043767 in view of Habener (U.S. Patent No. 5,120,712), Balschmidt et al (U.S. Patent No. 5,157,021), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742). The WO Patent Application '767 teaches oral administration of peptides such as insulin, salmon calcitonin, parathyroid hormone, lhrf, and GLP-1 linked to a membrane translocator using a

carrier comprising a pH-lowering agent, a protease inhibitor, an absorption enhancer, a non-physiologically active peptide, a gelatin capsule, and an enteric coating. See, e.g., page 17, lines 13-22, page 18, lines 10-27, page 20, lines 11-29, and claims 1-57. [Note that the WO Patent Application '767 does not designate the US, and therefore is not available as prior art under 35 U.S.C. 102(e).] The WO Patent Application '767 does not teach peptides which are amidated GLP-1 analogs, amidated insulin analogs, or amidated PTH analogs. Habener teaches GLP-1 analogs which are amidated. See, e.g., claims 1 and 4. Balschmidt et al teach insulin in which the carboxylic acid groups present in the sidechains at residues A4, A17, B13, and B21 are amidated in order to achieve a long-lasting protracted acting insulin analog. See, e.g., column 2, lines 5-8 and 49-53. Barbier et al teach the human parathyroid hormone derivatives hPTH(1-34)-OH and hPTH(1-31)NH_2, and teach that the derivatives can be administered orally. See, e.g., column 2, lines 26-44, and column 14, lines 59-62. The European Patent Application '201 teaches the human parathyroid hormone derivative hPTH(1-34)NH_2. See, e.g., column 3, lines 31-36. Neiss et al teach salmon calcitonin amidated at locations which are not naturally amidated and which have extended duration of activity. See, e.g., column 1, lines 42-44, and claims 1 and 2. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al in the oral administration compositions of the WO Patent Application '767 because the oral administration compositions have general applicability to any peptide and because it would be desirable to be able to administer orally the peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, and Neiss et al because oral administration is easier for the patient.

Applicants' claims would have been prima facie obvious at the time the invention was made because applying the WO Patent Application '767's known and generally applicable technique, i.e. of combining peptides with a pH-lowering agent, a protease inhibitor, an absorption enhancer, a non-physiologically active peptide, a gelatin capsule, and an enteric coating so that the peptides can be administered orally, to the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al, with only the expected result that the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al can be administered orally, is prima facie obvious. See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (S. Ct. 2007). With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

6. Claims 5 and 48 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 02/043767 in view of Habener (U.S. Patent No. 5,120,712), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742) as applied against claims 1-15, 17-41, 43-47, 49-53, 55-59, and 63 above, and further in view of Stern et al (U.S. Patent No. 5,912,014). Habener, Barbier et al, the European Patent Application '201, and Neiss et al teach known and specific peptides which are amidated at their C-termini, but do not teach synthesizing these peptides by forming glycine-extended precursors and then converting the glycine residue to a C-terminal amide group. Stern et al '014 teaches salmon calcitonin made with a C-terminal glycine extension which is enzymatically converted to an amide group. See, e.g., column 5, lines 12-23. It would have

been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the known and specific peptides of Habener, Barbier et al, the European Patent Application '201, and Neiss et al for use in the oral administration compositions of the WO Patent Application '767 by synthesizing the peptides as glycine-extended precursors and then converting the glycine residue to a C-terminal amide group, because Stern et al '014 teaches that this is a known reaction technique for forming a C-terminally amidated peptide, and because the particular method of synthesizing a peptide would not have been expected to affect the in vivo activity of the peptide.

7. Claims 1, 4, 5, 17-19, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by the Neugebauer et al article (Biochemistry, Vol. 34, pages 8835-8842). The Neugebauer et al article teaches a composition comprising hPTH(1-31)NH_2 combined with palmitoyloleoyl-phosphatidylserine vesicles in phosphate-buffered solution. See, e.g., page 8836, column 1, second full paragraph, and column 2, second paragraph; page 8839, Figure 7 and paragraph bridging columns 1 and 2. Note that an intended use limitation, e.g., "orally delivered", does not impart patentability to product claims where the product is otherwise anticipated by the prior art. Because the Neugebauer et al article teaches the only components specified in Applicants' claims, i.e. hPTH(1-31) amidated at its C-terminus and a phospholipid, inherently the composition of the Neugebauer et al article will provide enhanced bioavailability of the amidated peptide when it is orally delivered to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the compositions of the Neugebauer et al article and Applicants' claimed compositions to shift the burden to Applicants to provide evidence that the claimed compositions are unobviously different than those of the Neugebauer et al article.

With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

8. Applicant's arguments filed March 18, 2010 have been fully considered but they are not persuasive.

Applicants have clearly stated and explained why the instant claims do not embrace naturally occurring LHRH as the active peptide which has been amidated at a location that is not naturally amidated. Accordingly, the rejection under 35 U.S.C. 112, second paragraph, set forth in section 2, and the prior art rejections set forth in sections 6-9, of the Office action mailed September 18, 2009 are withdrawn. With respect to instant claim 61, note that this claim explicitly requires LHRH to be amidated at a location that is not naturally amidated. In light of Applicants' remarks, claim 61 requires LHRH to be amidated at a location other than at its C-terminus.

The obviousness rejections based upon Stern et al (U.S. Patent No. 6,086,918) or the WO Patent Application 02/043767, in view of Habener (U.S. Patent No. 5,120,712), Balschmidt et al (U.S. Patent No. 5,157,021), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, Neiss et al (U.S. Patent No. 4,804,742), or Stern et al (U.S. Patent No. 5,912,014), are maintained for the reasons of record. In particular, motivation to combine references under 35 U.S.C. 103 need not be the same motivation disclosed by Applicants for their invention (see MPEP 2144 and In re Dillon, 16 USPQ2d 1897 (Fed. Cir. 1990)). Further, there is no evidence of record, commensurate in scope with the rejected claims, establishing that amidation of a peptide at a location that is not naturally amidated unexpected increases the

bioavailability of the peptide. The only evidence of record establishing an unexpected increase in bioavailability is for PTH 1-34NH_2. The mere assertion of unexpected results for the entire genus of peptides is not sufficient to rebut the prima facie case of obviousness. With respect to the Stern declaration under 37 CFR 1.132 filed July 28, 2009, the examiner maintains his position for the reasons set forth in the Office action mailed September 18, 2009.

The anticipation rejection over the Neugebauer et al article (Biochemistry, Vol. 34, pages 8835-8842) is maintained. An anticipation rejection based upon the inherent presence of a claimed property is not rebutted by asserting that the reference does not teach or disclose the claimed property. In general, see MPEP 2112 and 2112.01. Although this does not affect the basis of the anticipation rejection, it should also be noted that the rejected claims do not explicitly state that the amidation is responsible for the promoted bioavailability.

9. The Information Disclosure Statement referred to at page 14, first full paragraph, of Applicants' Remarks has not been received by the time it became necessary to prepare this Office action.

10. Claims 42, 60, and 61 are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
June 3, 2010